REMARKS

Claims 1, 7-21 and 29-50 are pending. Claims 34-50 are withdrawn as being directed to a non-elected invention. Claims 1, 7-21, and 29-33 are rejected under 35 U.S.C. § 103(a) for obviousness over WO 99/01034 and WO 00/69449 in view of Keller et al. (Frontiers in Bioscience, 1996; hereinafter "Keller"), Hibberts et al. (Journal of Endocrinology, 1998; hereinafter "Hibberts"), and Van Nispen (U.S. Patent No. 5,002,881; hereinafter "Van Nispen"). By this reply, Applicants amend claims 20 and 21, and address each of the Examiner's rejections.

Support for the Amendment

The amendment to claims 20 and 21 is made to promote consistency between the pending claims. No new matter is added by the amendment.

Telephone Interview with Examiner Gough and Examiner Davis

Applicants wish to thank Examiners Gough and Davis for the telephonic interview of September 5, 2007. As was discussed during the telephonic interview, and as is discussed in more detail below, the cited references WO 99/01034, WO 00/69449, Keller, Hibberts, and Van Nispen, singly or in combination do not teach or suggest all of the limitations of present claims 1, 7-21, and 29-33. Applicants respectfully request reconsideration of the rejection of these claims under 35 U.S.C. § 103(a), and also request withdrawal of the finality of the present Office Action (please see the Petition to Withdraw Finality Under 37 C.F.R. § 1.181, enclosed herewith). If the Office does not agree, Applicants respectfully request that the Office contact the undersigned by

telephone in order to resolve any remaining issues in this case.

Rejections under 35 U.S.C. § 103(a)

WO 99/01034 and WO 00/69449 in view of Keller, Hibberts, and Van Nispen

Claims 1, 7-21, and 29-33 are rejected under 35 U.S.C. § 103(a) for obviousness over the combination of WO 99/01034, WO 00/69449, Keller, Hibberts, and Van Nispen. As was discussed during the telephonic interview, none of WO 99/01034, WO 00/69449, Keller, Hibberts, or Van Nispen, alone or in combination, teaches or suggests the preparation of culture medium that is conditioned by prostate epithelial cells, much less the use of such conditioned medium to culture hair inductive cells (e.g., dermal papilla cells and dermal sheath cells), as is required by present claim 1, and claims dependent therefrom.

Neither WO 99/01034 nor WO 00/69499 teaches or suggests culturing hair inductive cells in medium conditioned by prostate epithelial cells. WO 99/01034 only discloses culturing human dermal papilla cells using a culture medium that is supplemented with a conditioned medium "formed from the cultures of *normal human keratinocytes*" (see WO/99/01034, p. 4; emphasis added). WO 00/69499 merely discloses the use of various types of *stem cells* obtained from "many different tissue types" for preparing conditioned cell media (see WO 00/69499, p. 12, lines 13-20). Both WO 99/01034 and WO 00/69499 fail to teach or suggest the use of *prostate epithelial cells* to produce conditioned culture medium for <u>any purpose</u>.[1] WO 00/69499 describes the preparation of a different conditioned media, that is not used for cell culture, but for topical application to the skin to stimulate hair growth. This conditioned media is prepared using

1 Applicants note that the prostate epithelial cells of claim 1 are not stem cells.

dermal papilla cells, not prostate epithelial cells (see WO 00/69499, p. 45, line 34, through page 46, line 3). Thus, both WO 99/01034 and WO 00/69499 fail to teach or suggest preparing a culture medium that is conditioned by prostate epithelial cells, much less the use of this conditioned medium to supplement a culture medium that is used to cultivate hair inductive cells, as is recited in present claims 1, 7-21, and 29-33; this fact is acknowledged by the Office (see Office Action, p. 5).

To cure the deficiencies of WO 99/01034 and WO 00/69499, the Office cites Keller, Hibberts, and Van Nispen.[2] The Office states:

> It is known in the art that the development of the hair follicle depends on a mesenchymal-epithelial interaction, i.e., dermal papilla-keratinocytes. The same is true for prostate tissue, i.e. prostate stroma-prostate epithelial cells, as is disclosed by Keller...It is also known that androgen plays a role in the development of both. (Office Action, pp. 7-8.)

Based on Keller and Hibberts, the Office concludes:

> It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cultivated hair inductive cells such as dermal papilla cells in a medium conditioned with prostate epithelial cells because it is known in the art that both hair follicles and the prostate develop via mesenchymal-epithelial interactions, i.e dermal papilla-keratinocytes and prostate stroma-prostate epithelial cells and both hair follicle and prostate development are androgen modulated, plus there has been an observed association between men with male pattern baldness and benign prostate hyperplasia..., **therefore, one would expect to establish the required mesenchymal-epithelial interaction between dermal papilla cells and prostate epithelial cells required for hair follicle development**. (Office Action, pp. 8-9; emphasis added.)

Applicants respectfully traverse this rejection.

---

[2] As was noted in the previous Reply to Office Action, filed on January 22, 2007, Van Nispen is cited for its disclosure of ultrafiltration, which is an element of present claim 32 only (Office Action, p. 9). Because Van Nispen is not relevant to claims 1, 7-21, 29-31, and 33, for simplicity, Applicants only address the rejection of these claims over the combination of WO 99/01034, WO 00/69499, Keller, and Hibberts. Applicants note, though, that Van Nispen does not cure the deficiencies of WO 99/01034, WO 00/69499, Keller, and Hibberts with respect to claims 1, 7-21, and 29-33.

As was discussed during the telephonic interview, neither Keller nor Hibberts teaches or suggests culturing hair inductive cells in a medium conditioned by prostate epithelial cells, as is required by present claim 1, and claims dependent therefrom. Furthermore, one of skill in the art would not be motivated to culture hair inductive cells in a culture medium conditioned by prostate epithelial cells based on Keller or Hibberts, much less have any reasonable expectation that hair inductive cells cultured in this medium would expand: neither Keller nor Hibbert teaches or suggests that prostate epithelial cells could support the growth of hair inductive cells. The Office supports the present rejection by stating:

> One of ordinary skill in the art would have been motivated to condition a hair inductive cell medium with prostate epithelial cells to achieve a mesenchymal-epithelial interaction necessary for the development of hair follicles given that both prostate and hair cell development depend on this interaction and are androgen mediated. (Office Action, pp. 6-7.)

This conclusion is unsupported by the references or evidence.

No evidence of record suggests or provides any reasonable basis to conclude that prostate epithelial cells would be capable of supporting the growth of hair inductive cells, either directly or by culture in a medium conditioned by prostate epithelial cells. Nothing in the prior art suggests that prostate epithelial cells, either alone or by culture in a medium conditioned by these cells, would be effective in supporting the growth of hair inductive cells.

The Office asserts that the basis for this conclusion is found when Keller and Hibberts are combined with WO 99/01034 and WO 00/69499 because Keller and Hibberts disclose that prostate tissue and hair follicles "achieve a mesenchymal-epithelial interaction necessary for...development" (Office Action, p. 6). Thus, the Office concludes that the combination of these references leads to the conclusion that epithelial cells from prostate tissue will support the

growth of hair inductive cells from hair follicles (Office Action, pp. 6-7).

Nothing in Keller or Hibberts supports this conclusion, much less motivates the skilled artisan to use epithelial cells from prostate tissue to support the growth of hair inductive cells from hair follicles. In fact, Keller and Hibberts disclose that, notwithstanding the fact that prostate tissue and hair follicles exhibit similar epithelial-mesenchymal cell interactions, prostate tissue and hair follicles exhibit significant **tissue specific effects** that are unique to the distinct tissue environment in which these cells are found.

Keller reports that epithelial cells from prostate tissue and hair follicles respond to stimuli (e.g., exposure to androgens) with significantly different effects in these two tissues. In particular, Keller reports that androgens promote

> the differentiation of the urogenital sinus into the prostate, penis, and scrotum...[, while] the biology of hair growth offers an example of the **different effects** that androgens exert on the proliferation of similar populations of epithelial cells...Several lines of evidence support the role of androgens in controlling the growth of hair follicles...Taken together, these findings suggest that androgen, via the AR [androgen receptor], can indirectly mediate an effect on hair follicle proliferation through modulating dermal papilla activity. Though these data do not explain how T[estosterone] modulates cell proliferation in hair follicles, the differences in androgen metabolism and AR expression may, in part, account for the opposite proliferative responses observed in various epithelial tissues. The effect of androgens on cell proliferation in hair follicles may be regulated through regulation of expression of growth factors. Androgens can modulate expression of a variety of growth factors in the prostate stroma. (Pages 62-63; emphasis added.)

In addition, Keller observes that "[a]ndrogens can modulate expression of a variety of growth factors in the prostate stroma", which can result in the development of prostate carcinoma cells (see Keller, p. 63).

Hibberts, like Keller, states that the regulation of epithelial cells in hair follicles is different from the regulation of epithelial cells in prostate tissue and produces different effects.

Specifically, Hibberts reports that "androgens act on the epithelial cells of the hair follicle via the mesenchyme-derived dermal papilla, causing stimulation of some hair follicles (e.g. beard) whilst inhibiting others, as in male pattern baldness, altering the production of regulatory factors" (p. 64). Thus, both Keller and Hibberts show that, notwithstanding the presence of an epithelial-mesenchymal cell interaction, prostate tissue and hair follicles exhibit distinct **tissue specific effects** in response to stimuli (e.g., exposure to androgens) that results in, in particular, the expression of different growth or regulatory factors. Because prostate tissue and hair follicles were known to respond differently to stimuli, one skilled in the art would not be motivated, based on Keller or Hibberts, to culture hair inductive cells in a culture medium conditioned by prostate epithelial cells, nor would the skilled artisan have any reasonable expectation that a culture medium conditioned by prostate epithelial cells would successfully promote the growth of hair inductive cells in culture.

Applicants respectfully submit that WO 99/01034, WO 00/69499, Keller, Hibberts, and Van Nispen, either alone or in combination, fail to teach or suggest the invention of present claims 1, 7-21, and 29-33, fail to provide any motivation to culture hair inductive cells in medium conditioned by prostate epithelial cells, and provide no reasonable expectation that culturing hair inductive cells in medium conditioned by prostate epithelial cells would be successful. For these reasons, the rejection of claims 1, 7-21, and 29-33 should be withdrawn.

CONCLUSION

In view of the above remarks, Applicants respectfully submit that the present claims are in condition for allowance, and such action is respectfully requested.

If there are any additional charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

TODD ARMSTRONG, Ph.D.
Reg. No. 54,590

Date: 21 December 2007

For Paul T. Clark
Reg. No. 30,162

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045